Breaking the barrier: Plasmodium knowlesi can adapt to infect Duffy-negative Erythrocytes

Plasmodium knowlesi, a zoonotic malaria species, has become a significant public health concern in Southeast Asia. Despite progress in eliminating other human malaria parasites in Malaysia and southern Thailand, *P. knowlesi* cases have surged. Like *Plasmodium vivax, P. knowlesi* relies on Duffy-Antigen Receptor for Chemokines (DARC) in invading human erythrocytes and is thought to affect only Duffy-positive individuals. However, our current research demonstrates *P. knowlesi's* surprising invasion adaptability. We found that this parasite can overcome its dependence on DARC, adapting in lab conditions to invade and replicate within Duffy-negative (Fy-) erythrocytes. This adaptation, unrelated to DARC binding, remains stable and unaffected by α-DARC antibodies. Genomic analysis revealed a recombination between the parasite's similar genes, *dbpα* and *dbpγ*, creating a new chimeric gene. Through targeted genetic reversal, we confirmed its necessity for invading Duffy-negative erythrocytes. This discovery sheds light on *P. knowlesi's* invasion plasticity, vital for understanding its potential transmission beyond Southeast Asia and the intricate host cell tropism of *P. vivax*. This insight into atypical invasion pathways holds significance for malaria research and potential future interventions.